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*Brief Clinical Report*

# Hypertrichosis, Pigmentary Retinopathy, and Facial Anomalies: A New Syndrome?

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**We report on a 22-month-old male with congenital hypertrichosis of the face, arms, legs, shoulders, back, and buttocks, abnormal facial appearance, dolichocephaly, and pigmentary retinopathy. Symmetrical hyperpigmentation is present on the sideburn areas of his face, and hyperpigmented streaks are seen on arms and legs. Biopsy of the hyperpigmented skin showed many separate bundles of smooth muscles in the dermis. No relative had hypertrichosis or other birth defects. To our knowledge, the syndrome of facial anomalies, pigmentary retinopathy, and congenital hypertrichosis has not been reported previously.**



**KEY WORDS: congenital hypertrichosis, pigmentary retinopathy, facial dysmorphia**

## INTRODUCTION

Congenital hypertrichosis is rare, heterogeneous, and is characterized by excessive growth of hair over most of the body [Suskind and Esterly, 1971]. The disorder is usually due to an autosomal dominant gene [Freire-Maia et al., 1976], but autosomal recessive transmission has also been observed. A number of sporadic cases have also been reported [Ray, 1966]. Some patients have associated osteochondrodysplasia [Cantú et al., 1982], and others have cone-rod amaurosis [Jalili, 1989]. One multi-generational pedigree suggested X-linked dominant inheritance [Macías-Flores et al., 1984]. The case described herein seems to be a distinct form of congenital hypertrichosis associated with facial anomalies and pigmentary retinopathy.

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## CLINICAL REPORT

The propositus was the product of the second pregnancy of a non-consanguineous 27-year-old black mother and a 29-year-old black father. Their first pregnancy resulted in the birth of a healthy girl. The mother denied taking any medication, drinking alcohol, or exposure to toxins. She smoked a half pack of cigarettes a day. The family history was unremarkable. Delivery was at 36 weeks gestation. Birth weight was 2,800 g (60th centile), crown-heel length was 48 cm (60th centile), and head circumference (OFC) was 34 cm (80th centile). At birth, the infant was noted to have an abnormal facial appearance with a striking amount of long, dark hair covering most of his body.

On physical examination, at 2 months, the child was small for age, length was 50 cm (5th centile), weight was 3,850 g (25th centile), and head circumference was 38 cm (25th centile). He had sunken cheeks, wide nasal bridge, prominent infraorbital creases, and large downturned mouth. There was symmetrical skin hyperpigmentation on each sideburn area (Fig. 1). Hypo- and hyperpigmented streaks were present on arms and legs (Fig. 2). Excessively long, fine darkly pigmented hair covered shoulders, back, buttocks, arms, and legs (Fig. 3). There was minimally increased growth of hair over the chest and abdomen. There was no sexual hair development. Palms, soles and mucous membranes had no hair growth. Dermatoglyphic analysis of digital patterns (1–5) on the right hand are ulnar, ulnar, radial, arch, and ulnar. The right axial triradius is distal (2/4). On the right hallucal area is a loop distal. On the left hand, digits are arch, whorl, ulnar, arch, and ulnar. A loop distal is present in the 3rd interdigital space. On the left hallucal area is also a loop distal.

Chromosomes of lymphocytes and skin fibroblasts were apparently normal karyotype (46,XY). Skeletal survey showed no abnormality and bone age was compatible with chronological age. Intracranial ultrasonography showed normal brain structure, except for a small, unilateral choroid plexus cyst.

Ophthalmic examination documented hypertelorism, long eyelashes, left hypertropia associated with left cranial nerve IV palsy, hyperopia, and a diffuse bilateral mottled pigmentary retinopathy. About each optic nerve head was an area of dense hyperpigmentation.

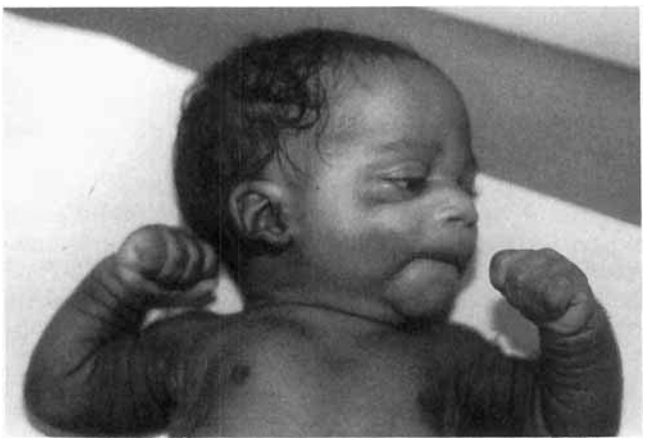

Fig. 1. Side view of face, age 2 months. Note hyperpigmentation on sideburn area.

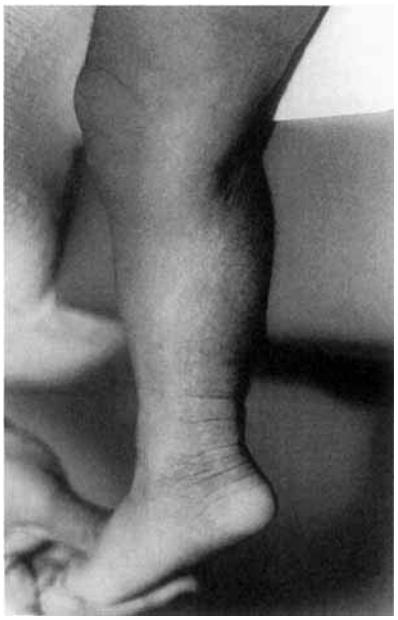

Fig. 2. Note longitudinal hypopigmented area along the leg.

The optic nerves and retinal vessels appeared normal. The child had good vision with steady fixation using a right head turn and chin down position.

At 22 months, the hypertrichosis was unchanged. He had well-demarked normal scalp hair, eyebrows and excessively long eyelashes (Fig. 4). His general health remained excellent. Early motor development was delayed. He first sat without support at 1 year. He was able to walk without support at 22 months at which time he had only a 3-word vocabulary.

Laboratory examinations included complete blood count, serum electrolytes and glucose urinalysis, lipid profile, and liver functions—all with normal or negative results. The skeletal radiograms revealed an asymmetrical skull, but no other sign of skeletal dysplasia. The computerized tomography of the head showed normal brain structure and good gray-white matter differentiation. Hair biopsy of left arm with 3 mm punch was done at 20 months. Hematoxylin and eosin stain showed many smooth muscles in separate bundles without attachment to the hair follicle (Fig. 5).

## DISCUSSION

Congenital hypertrichosis is usually categorized as either lanuginosa or terminalis. Congenital hypertri-

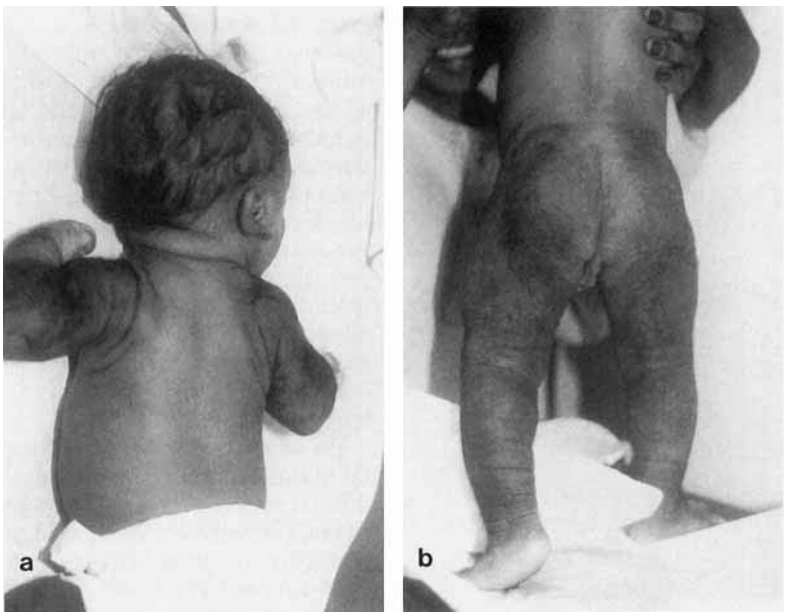


Fig. 3. Hypertrichosis on shoulders, arms (**a**), and legs and buttocks (**b**) at age 2 months.

Fig. 4. Facial appearance of patient at age 22 months.

chosis lanuginosa or congenital universalis is a rare heterogeneous group of disorders. This disorder was first described by Aldrovandus [1642]. During the last century, the few known cases drew considerable attention from the public when some of these individuals were exhibited for money in circuses or market places [Bondeson and Miles, 1993].

In congenital hypertrichosis lanuginosa the individual's skin surface, including the face, is covered by long, wavy, silky lanugo hair. Palms, soles, and mucous membranes are spared. The pubic, axillary and beard areas retain lanugo hair at puberty and terminal hair does not appear. It is thought that this condition may be due to a developmental arrest resulting in persistence of embryonic hair [Storer and Hawk, 1988].

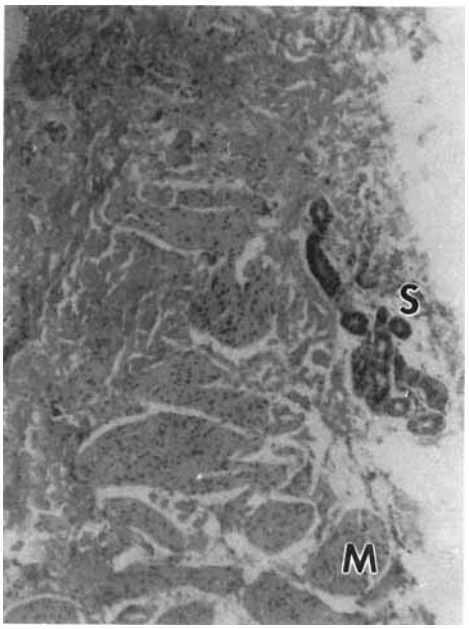


Fig. 5. There are many distinct, separate bundles of smooth muscle (M). There is no connection of these muscles with hair in this field. Eccrine sweat gland (S) (Hematoxylin-eosin stain, ×120).

Congenital hypertrichosis lanuginosa is to be differentiated from *congenital hypertrichosis terminalis*. In hypertrichosis terminalis the affected individuals have terminal hair growth over the body but the facial hair distribution follows a more normal male pattern. This type of hypertrichosis has been associated with gingival hypertrophy and "simian facial characteristics" [Ray, 1966]. Hypertrichosis terminalis is presumably secondary to general defects in hair growth suppression [Porter, 1971]. Congenital hypertrichosis lanuginosa and congenital hypertrichosis terminalis have both been reported as autosomal dominant disorders with variable manifestations [Freire-Maia et al., 1976]. X-linked dominant inheritance was observed in the multi-generational family by Macías-Flores [1984]. The gene responsible for this latter type of hypertrichosis was recently mapped to Xq24→q27.1 [Figuera et al., 1995]. Clinical data and associated anomalies of eight previously reported patients with generalized hypertrichosis are summarized in Table I.

Congenital hypertrichosis (both general categories) has been associated with other congenital abnormalities such as osteochondrodysplasia and dental defects [Cantú et al., 1982]. A number of congenital ophthalmological anomalies have been reported in patients with congenital hypertrichosis including cone-rod amaurosis [Jalili, 1989], ectropion [David, 1991], glaucoma [Judge et al., 1991], and cataracts [Temtamy and Sinbawy, 1991]. The pathogenesis of congenital hypertrichosis is unknown. No endocrine or metabolic abnormalities are known.

In our patient, the simultaneous occurrence of congenital hypertrichosis with facial anomalies and pigmentary retinopathy suggests an ectodermal disturbance during embryonic life due to the pleiotropic effect of the disease-causing gene. Our patient has an unusual facial appearance with sunken cheeks and apparent decrease in subcutaneous fat, particularly in the buttocks region. These findings raise the possibility of lipodystrophy. The hallmarks of lipodystrophy include generalized absence of body fat, increased skeletal growth, acanthosis nigricans, enlarged external genitalia, hepatomegaly, and insulin-resistant diabetes [Benardinelli, 1954]. Our patient had only the regional decreased subcutaneous fat (face and buttocks). There was no evidence of elevated blood sugar or hypertriglyceridemia.

He also has trichomegaly, high hyperopia, unilateral IV nerve palsy, and pigmentary retinopathy. Other conditions such as Oliver-McFarlane syndrome which are characterized by trichomegaly, pigmentary retinopathy and growth retardation can be distinguished from the condition of our patient due to the presence of generalized hypertrichosis [Chang et al., 1993].

The persistent hypertrichosis in our patient is most extensive on the shoulders, arms, legs, and buttocks.

TABLE I. Abnormalities Associated With Congenital Generalized Hypertrichosis*

| Disorder | Congenital hypertrichosis lanuginosa (CHL) | | | | Congenital hypertrichosis terminalis (CHT) | | | Congenital hypertrichosis non-classified | |
|---|---|---|---|---|---|---|---|---|---|
| Reference no. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Inheritance | AD/AR? | AR | AR | AR | AD | AD | ? | AR | AR |
| Hair phenotype | Lanugo[a] | Lanugo | Lanugo | Lanugo | Terminal[a] | Terminal | Terminal[a] (arrector pili muscle hamartoma) | N/M | N/M |
| Skeletal/other anomalies | Dental defects | N/M | Microdontia | Macrostomia atrophic skin | Simian characteristics gingival fibromatosis | N/M | Craniofacial | Osteochondro-dysplasia | N/M |
| Eye anomalies | N/M | Glaucoma | Cataract | Ectropion | N/M | N/M | Pigmentary retinopathy | N/M | Cone-rod dystrophy |

* N/M, not mentioned. 1, Suskind et al. [1971]; 2, Judge et al. [1991]; 3, Temtamy et al. [1991]; 4, David et al. [1991]; 5, Bondeson et al. [1993]; 6, Macias-Flores et al. [1984]; 7, Present case; 8, Cantú et al. [1982]; 9, Jalili et al. [1989].
[a] Microscopic hair analysis.

The face has a peculiar hyperpigmentation on the sideburn areas. Hypo- and hyperpigmented streaks were present on the arms and legs. The patches of normal and abnormal skin pigmentation follow Blaschko lines. This pattern is seen in several X-linked skin conditions in which mosaicism in females is due to random X inactivation; examples include incontinentia pigmenti, Goltz syndrome, and X-linked hypohydrotic ectodermal dysplasia [Happle, 1985]. Blaschko line pigmentation is also seen with chromosomal mosaicism [Moss et al., 1993]. In our case there was no evidence of chromosome mosaicism in the fibroblasts or lymphocytes. Histologically, there are many smooth muscles beneath the hypertrichotic skin. This histological picture is compatible with smooth muscle hamartoma in which separate, mature smooth muscles are scattered in the dermis with or without attachment to hair follicles. The presence of hypertrichosis and hyperpigmentation has been described in some smooth muscle hamartomata [Zvulunov et al., 1990]. In Becker's melanosis, the hyperpigmentation, hypertrichosis, and, in some cases, increased numbers of smooth muscles are combined [Hashimoto et al., 1987]. However, in smooth muscle hamartoma and Becker's melanosis, the lesion is localized, unlike our patient who has a generalized distribution.

Our patient presents yet another variation of phenotypic abnormalities associated with hypertrichosis. Not only is the hypertrichosis unusual (distribution of face to shoulders with underlying smooth muscle masses), but the associated anomalies (regional lipoatrophy, developmental delay, abnormal skin pigmentation, ocular anomalies) widen the clinical spectrum. Hopefully, through reporting patients with hypertrichosis and malformations, a clearer clinical categorization will evolve.

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